REMARKS

This paper is filed in response to the office action mailed on December 28, 2004. In the office action, the restriction requirement is made final, and therefore claims 29-37 are withdrawn. Claims 1, 3-5, 9-11, 15-28, and 38-41 are pending.

Claims 1, 3-5, 9-11, 15-28, and 38-41 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Krall et al. WO 00/44287 ("Krall") in view of Slaikeu et al. U.S. Patent No. 6,160,025 ("Slaikeu"). Applicant respectfully submits that this rejection is improper because no combination of Krall and Slaikeu establishes a *prima facie* case of obviousness.

Under M.P.E.P. §§ 2142 and 2143, to establish a case of obviousness, three criteria must be met. First, there must be a suggestion or motivation in the references cited or in the general knowledge of the art to modify the references or combine the teachings of the references. Second, there must be a reasonable expectation for success that the proposed modification or combination would work. Third, the proposed combination of references must teach or suggest all of the claim limitations. Applicants respectfully submit that there is no suggestion or motivation to combine Krall and Slaikeu, and, further, a combination of Krall and Slaikeu fails to teach or suggest every limitation of the claims. Hence, the proposed combination fails to establish a *prima facie* case of obviousness, for at least two reasons.

Claim 1 recites a medical composition comprising (1) a matrix-forming component of alkyl cyanoacrylate monomers, a stabilizer, and a plasticizer; (2) a solid aggregate material that includes a radiopacificer; and (3) a polymeric non-cyanoacrylate rheology modifying agent with a molecular weight greater than 200,000.

Krall teaches of an embolic composition comprising an alkyl cyanoacrylate monomer, at least one inhibitor, an alkyl esterified fatty acid and an opacificant agent. The Patent Office admits at page 4 of the Office Action that Krall does not teach or suggest the use of a polymeric non-cyanoacrylate rheology modifying agent having a molecular weight of greater than 200,000.

The Patent Office then looks to Slaikeu to supplement this deficiency of Krall. However, Slaikeu teaches an embolic composition comprising a liquid solution of partially hydrolyzed polyvinyl acetate polymer that precipitates and agglomerates, along with a pharmaceutically acceptable solvent and optionally a radiopacifier. The Patent Office

contends that the use of the partially hydrolyzed polyvinyl acetate polymer is analogous to the applicant's polymeric non-cyanoacrylate rheology modifying agent, and, therefore, the applicant's application is unpatentable over Krall in view of Slaikeu. However, because the Slaikeu polyvinyl acetate polymer is used as an agglomerant and not a rheology modifying agent, applicant respectfully traverses.

Slaikeu teaches a partially hydrolyzed solution of polyvinyl acetate polymer in an appropriate solubilizing solvent, not as a rheology modifying agent. The Slaikeu solution is introduced to an appropriate mammalian site, whereupon the solubilizing solvent is dispersed and/or diluted once in contact with the aqueous medium of the site of interest. This causes the solubilized partially hydrolyzed polyvinyl acetate polymer to precipitate out of solution, agglomerate and form a embolizing agent. See column 4, lines 30-36 of Slaikeu.

The discussion in Slaikeu of viscosity of various molecular weight polymers of partially hydrolyzed polyvinyl acetate is not relevant to the applicant's use of non-cyanoacrylate rheology polymers above a molecular weight of 200,000. Specifically, Slaikeu only discusses molecular weight in connection with the necessity of having a solution of a manageable viscosity for introduction through a syringe or cannula. See column 5, lines 1-26, and column 8, examples 8-10, with particular interest in example 10, wherein a partially hydrolyzed polyvinyl acetate of molecular weight 300,000 was found to be too viscous for use with a number 3 French diameter syringe, with the concomitant conclusion that polymers of under 300,000 molecular weight are necessary for successful injection with a syringe.

Slaikeu is silent on the use of non-cyanoacrylate polymers as rheology modifying agents in a composition containing another agglomeration matrix forming component, inhibitor, and plasticizer. Slaikeu teaches the use of the polyvinyl acetate as the matrix forming or agglomerating ingredient instead of applicant's cyanoacrylate monomers or Krall's alkyl cyanoacrylate.

Furthermore, there is no motivation within Slaikeu to combine its partially hydrolyzed polyvinyl acetate composition with another polymerizing agent or composition as taught by Krall, as the Slaikeu mechanism for forming an agglomeration or embolic agent is vastly different from the mechanism used by Krall. Krall uses alkyl cyanoacrylate monomer, and a host of other ingredients, to form an aggregate in an anionic environment. In contrast, Slaikeu starts with already polymerized polyvinyl acetate whose solubility has been manipulated using a pharmaceutically acceptable solvent, that, upon entry to the mammalian

site of interest, changes solubility and precipitates out of solution and agglomerates. Slaikeu does not teach or utilize any polymerization. In contrast, Slaikeu only teaches of partially hydrolyzed polyvinyl acetate polymers as agglomeration agents because it is the special solubility properties of these polymers (and only at specific molecular weights) that is key to their invention. No other polymer is mentioned as a possible replacement or substitute for their teachings, as the solubility properties are vital to success using their techniques.

Thus, there is no motivation to combine the teachings of Krall with those of Slaikeu as each is concerned with a self-contained manner in creating an embolic agent, once delivered to the appropriate site. The use of partially hydrolyzed polyvinyl acetate in Slaikeu is, in and of itself, the method of forming an agglomeration agent. It is neither taught nor suggested that such a moiety would or could be used successfully in a cyanoacrylate monomer matrix to advantageously modify the rheological properties of a potential embolic agent. A person of skill in the art would have no motivation to combine the teachings of Krall (i.e. using monomers of cyanoacrylate that, once in the body, polymerize to form an embolic agent) with those of Slaikeu (already polymerized entities whose solubility properties have been manipulated to agglomerate once in the body) as these two approaches to forming embolic agents work through vastly different mechanisms.

Furthermore, even if combined, the teachings of Krall and Slaikeu would not meet all the limitations of claim 1. Slaikeu's partially hydrolyzed polyvinyl acetate performs the same function as Krall's cyanoacrylate monomers as the agglomeration agent, and therefore, a combination of the Krall and Slaikeu would still leave unaccounted applicant's rheology modifying agent because one of ordinary skill in the art would use Slaikeu's polyvinyl acetate as a substitute for Krall's cyanoacrylate. Therefore, no *prima facie* case of obviousness can be made from the combined teachings of Krall and Slaikeu.

The Patent Office further supplements Krall and Slaikeu with U.S. Patent No. 4,997,861 ("Hechenberger"). However, Hechenberger merely teaches of a cyanoacrylate monomer combined with an alkyl acrylate, fumed silica and a polymerization stabilizer for use as an instant adhesive composition. The function of this adhesive is for industrial purposes, and for use on "porous substrates such as paper, cardboard, leather, and wood." See column 1, lines 14-15 and 23-27. The current application is concerned with *medical* applications of modified and supplemented cyanoacrylate matrices. There is no motivation or suggestion to combine the teachings of Hechenberger with either Krall or Slaikeu. Even if

combined, the various teachings would not establish a *prima facie* case of obviousness, as none of the documents discuss the use of a rheology modifying agent to increase the viscosity of the mixture to form a better embolic composition.

In view of the above arguments, it is submitted that the pending application is in condition for allowance and an early action so indicating is respectfully requested.

The Commissioner is authorized to charge any fee deficiency required by this paper, or credit any overpayment, to Deposit Account No. 13-2855.

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Respectfully submitted,

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